Did our fabrication process impact on azacitidine stability?

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Introduction

Azacitidine stability depend on reconstitution temperature of water for injection (WFI) and on vial temperature. In routine production, our process includes 15 minutes of decontamination with peracetic acid at 45°C and transfer of the preparation to ward and finally administration to the patient is usually done more than one hour after the beginning of the preparation. Elevation of temperature (T°C) may occur along the process compromising the stability of azacitidine. So, our goal was to monitor temperature during the whole process and to assess the stability of azacitidine in real life condition.

Materiel and methode

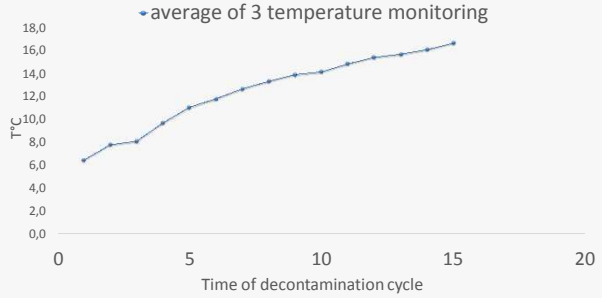
T°C of vials was monitored during 3 different decontamination cycle with temperature sensor (VWR®).T°C of water before and after sterilization for 20 ml and 250 flasks is kept with partial immersion thermometer (Brannan®).
All temperature measurements were done in triplicate.
Azacitidine syringe 25mg/ml were prepared as usually, concentration were determined by HPLC–UV stability indicating method, immediately after reconstitution T0, T+30 minutes, T+45 minutes and T+1-hour store at ambient temperature, and on one syringe returned from ward (cold chain not respected).

Resultat et discussion

WFI Flasks T°C

	Before decontamination	At the end of decontamination
20ml flask	10°C	18°C
250ml flask	4°C	10°C

Temperature evolution in vials



Azacitidine concentration variations :

- Maximal variation after compounding : **-11,6%** at T +45 min.
- Returned syringe variation was : -**18.8% .**

Conclusion

Elevation of temperature occurs in the water for injection flask and in vials.

- Immediate corrective measure was implemented : **exclusion of 20 mL WFI flasks for reconstitution of azacitidine**
- Operators were reminded about good process for this drug (i.e. **immediate storage in fridge after preparation and systematically discarded if returned from ward**).

Additional tests are on going to assess whether or not we have to use BSC instead of isolator due to temperature elevation during the sterilization process.